Remarks

Claims 1, 4, 5, 7-11, and 14-18 are pending in this application.

I. Rejection Under 35 U.S.C. § 103

Claims 1, 4, 5, 7-11, and 14-17 are rejected under 35 U.S.C. 103 as being unpatentable over Gargano et al. Applicants respectfully traverse this rejection.

The instant application discloses "screening of entire antibody libraries, such as phage libraries, without prior application of phage display to isolate the antibodies which bind to the desired antigen" (see page 28, lines 29-33 and Example 4 on page 38). The Examiner appears to appreciate that Gargano et al fails to teach screening without prior application of phage display, as required by the claims, noting that Gargano et al. "is silent in teaching that no prior application of a phage display is [necessarily] used to isolate immunoglobulins that bind to a target," but then contends that Gargano suggests this limitation on page 176, second full paragraph, in referencing the following quotation from Gargano et al: "if scFV fragments can be successfully expressed in a yeast two hybrid format, monitoring their [stable] interaction with a corresponding [target] antigen should allow isolation of those scFV fragments that bind successfully to the antigen under intracellular expression conditions" (bracketed text supplied by the Examiner).

It is respectfully submitted that a fair reading of the Examiner's quote from Gargano et al, when considered in the context of the paragraph from which the Examiner has isolated it, would have led the person of ordinary skill to conclude that not only does Gargano et al fail to suggest that expression of scFV fragments could be done successfully in a yeast two hybrid format without prior application of phage display, but also to conclude that Gargano et al, in fact, suggests just the opposite: that expression of scFV fragments could be done successfully in a yeast two hybrid format only with prior application of phage display.

The rest of the second full paragraph of Gargano et al, following the Examiner's quote, discusses the use of prior application of phage display to extend the proof of concept to possible expression of scFV fragments in a yeast two hybrid format. Gargano et al discusses the hypothesis of "…extend(ing) to the analysis in the two hybrid format of small polyclonal repertoires selected from phage display antibody libraries by panning against a given antigen…

The major applications of such a scheme would be that of preselecting antigen-specific scFVs before their subsequent validation and exploitation in functional intracellular antibody experiments."

The last sentence confirms that Gargano et al in fact suggests a method wherein preselection steps are required and essential to enrich from the phage library for antibodies that bind the relevant antigen in vitro, for the subsequent validation step, which is the yeast two hybrid assay that is performed on an individual basis, one antibody at a time. Gargano et al also teaches that each successive cycle or step of preselection further enriches the pool of affinity purifed scFv fragments (see page 174, end of 3rd paragraph, page 176, 2nd full paragraph, page 177, 4th full paragraph, page 183, 1st paragraph, page 185, 1st paragraph and Figure 10.2).

Therefore, it is respectfully submitted that, when considered in the proper context, Gargano et al suggests that scFVs could be successfully expressed in a yeast two hybrid format, if preselected from phage display libraries.

In contrast, Applicants are claiming a method of direct selection of intracellular antibodies from a library, wherein selection is not carried out on an individual basis and antibodies are not preselected from a phage library. Applicants show that direct selection of scFv libraries in a yeast antibody-antigen system, without any preselection to reduce the size of the library, is feasible (see Example 4).

Further, Applicants respectfully disagree with the Examiner's characterization of the invention as the discovery of optimum workable conditions of the methods disclosed in Gargano et al. Gargano et al teaches the need for preselection steps to first enrich the population for phages that are able to bind the antigen of interest *in vitro*. The disclosure of Gargano et al, especially the fourth full paragraph on page 177 and Figure 10.2, suggests to one of skill in the art that more preselection steps, not fewer steps, would be optimum for removing irrelevant phages while enriching and amplifying those harboring antibodies that bind the antigen. Therefore, to optimize the working conditions of Gargano et al, one of skill in the art would have tried more preselection steps, not fewer. Applicants respectfully submit that Gargano et al in fact teaches away from what Applicants have shown, which is the direct selection of scFv libraries in a yeast antibody-antigen system, without any preselection to reduce the size of the library.

In summary, Applicants submit there is no teaching or suggestion in Gargano et al of how one of skill in the art would carry out successful expression of scFV fragments without preselection steps. Further, there is no support in Gargano et al. for the additional bracketed concepts supplied by the Examiner in quoting from that reference, which concepts are, in fact, derived in hindsight from the Applicants' specification, and not from the reference. Without such teaching or suggestion, it would not have been obvious for the skilled artisan to figure out how the two hybrid assay could be used for the successful direct selection of intracellular antibodies of unknown binding capacity, which is what Applicants have shown for the first time. Gargano et al. actually teaches away from any suggestion that expression could be successful without prior application of phage display to preselect antigen-specific scFVs.

Accordingly, Applicants respectfully submit that this rejection has been overcome and request that this § 103, first paragraph, rejection be withdrawn.

II. Conclusion

Applicants believe that the application is in condition for allowance. However, if the Examiner disagrees, the Examiner is encouraged to call the undersigned at the number listed below in order to expedite the prosecution of this application.

No fees are believed due; however, the Commissioner is authorized to charge any other necessary fees, or credit any overpayments, to our Deposit Account No. 08-0219, under Order No. 2202417.00120US1 from which the undersigned is authorized to draw.

Respectfully submitted,

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